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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,428	05/05/2006	Wolfgang Barnikol	BARNIKOL-3 PCT	2824

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EXAMINER	
HOBBS, LISA JOE	
ART UNIT	PAPER NUMBER
1657	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,428	BARNIKOL, WOLFGANG	
	Examiner	Art Unit	
	Lisa J. Hobbs	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05 May 2006, 08 Dec 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a certified English translation of the foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Information Disclosure Statement

The information disclosure statement(s) (IDS) submitted on 05 May 2006 and 08 December 2006 is/are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Status

Claims 2-9 are active in the case. Claim 1 has been cancelled by preliminary amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim9, with dependent claims 2-5 and 7-8, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "chemically modified" could have a

number of meanings, including merely that the hemoglobin hyperpolymer is chemically modified in itself because it is in a hyperpolymer. For the purposes of this examination, in light of the disclosure, the examiner is interpreting "chemically modified" to mean that a chemical such as a polyalkene oxide (PEG) is added to the hemoglobin multimer. Clarification of this description in the claim "chemically modified high molecular weight crosslinked hyperpolymer hemoglobin" is requested in order to appropriately disclose the metes and bounds of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nho et al. (US 5,234,903) and Winslow (US 6,432, 918) in view of Grinstaff et al. (US 5,665,383). Nho et al. teach chemically modified hemoglobin which is administered to support enhanced oxygen

transport to a patient in need thereof using physiological compositions, wherein the conditions include acute respiratory. They teach that the viscosity of hemoglobin may be altered by using polyakylene oxides so that maximal oxygen release may be obtained for the pateint (cols. 17 and 18). Winslow teaches compositions containing one or more of the following properties: i) viscosity at least half that of blood, ii) oncotic pressure higher than that of plasma; iii) hemoglobin oxygen affinity higher than or equal to (i.e., P50 equal to or lower than) that of blood; and iv) oxygen capacity less than that of blood. It is not intended that the invention be limited to how the compositions are used. A variety of uses are contemplated for the compositions of the present invention, including, but not limited to, the treatment of hemorrhage or use in hemodilution (paragraph 21). Specifically, Winslow teaches an oncotic pressure of less than 28 mmHg (paragraph 30). Winslow also teaches that the hemoglobin within the composition is surface-modified. It not intended that these embodiments be limited to any particular type of surface modification. In preferred embodiments, the surface modification includes the use of polyalkylene oxide groups of varying chain lengths and charges. In preferred embodiments, the hemoglobin is surface-modified with polyethylene glycol of varying chain lengths and charges. It is not intended that the surface modification be limited to any particular type or a single type of modification. It is contemplated, that multiple types of surface-modifications will be made to hemoglobin of the composition (paragraph 32). Also taught is that for medical administration as a blood supplement, the chemical modification to hemoglobin is generally one of intramolecular crosslinking and/or oligomerization to modify the hemoglobin such that its persistence in the circulation is prolonged relative to that of unmodified hemoglobin, and its oxygen binding properties are similar to those of blood. Intramolecular crosslinking

chemically binds together subunits of the tetrameric hemoglobin unit to prevent the formation of dimers which, as previously indicated, are prematurely excreted (paragraph 15). Grinstaff et al. teach that insoluble crosslinked hemoglobin avoids toxicity associated with soluble hemoglobin compositions of the prior art. Nephrotoxicity or renal toxicity of hemoglobin is mainly related to the clearance of soluble dimeric, tetrameric, or oligomeric hemoglobin from the circulation. The hemoglobin of the instant invention, being extensively crosslinked or `megameric`, cannot be cleared by the kidney and is unlikely to be nephrotoxic. The insoluble constructs of the instant invention cannot be cleared by the kidneys and therefore circumvent this problem. An additional advantage of the extensively crosslinked hemoglobin constructs of the present invention over the prior art is the increased intravascular persistence due to the insoluble form (paragraph 82).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Nho et al., Winslow and Grinstaff et al. to achieve the invention as claimed. Each of the references teaches intravascular administration of aqueous hypooncotic solutions, below 28 mmHg, comprising physiological components, such as saline, comprising chemically modified hemoglobin. Also taught is that HMW crosslinked hyperpolymers of hemoglobin are desirable to reduce toxicity to the kidney and that in addition to crosslinking between hemoglobin molecules one would desire to add various chemical modifications such as polyakylene oxides in order to increase size and affinity for oxygen. The hemoglobin may be obtained from various sources including humans, bovine or other animals. Since the prior art clearly discloses that many embodiments are possible, one of skill would have a reasonable expectation of success. Motivation for performing these modifications to

hemoglobin and using it for administration to a patient in need thereof is provided by the increased oxygen available to the patient and increased prognosis for health.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-16 of U.S. Patent No. 6,956,025. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite methods of treating patients in need thereof with crosslinked hemoglobin intravascularly in a physiologically compatible solution. While the instant application recites a hyperpolymeric hemoglobin and the '025 claims does not, the '025 patent not specifically exclude a hemoglobin derivative which is crosslinked and in a multimer configuration (see claim 1).

Claims 2-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-17 of U.S. Patent No. 7,005,414. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite methods of treating patients in need thereof with crosslinked hemoglobin intravascularly in a physiologically compatible solution. While the instant application recites a hyperpolymeric hemoglobin and the '414 claims does not, the '414 patent not specifically exclude a hemoglobin derivative which is crosslinked and in a multimer configuration (see claim 13).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Hobbs whose telephone number is 571-272-3373. The examiner can normally be reached on Monday to Friday, 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lisa J. Hobbs/
Primary Examiner
Art Unit 1657

ljh